

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/GB2004/002659

International filing date (day/month/year)
21.06.2004

Priority date (day/month/year)
19.06.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/4425, A61K35/56

Applicant
ABERDEEN UNIVERSITY

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4485

Authorized Officer

Friederich, M
Telephone No. +49 89 2399-7860



IAP20 Rec'd PCT/PTO 19 DEC 2005

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**International application No.
PCT/GB2004/002659**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search : (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002659

Box No. II Priority

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. ☐ It has not been possible to consider the validity of the priority claim because a copy of the priority document was not available to the ISA at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.
4. Additional observations, if necessary:

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WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITYInternational application No.
PCT/GB2004/002659**Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 1-11 and 21-29 with respect to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 1-11 and 21-29 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. -
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

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**WRITTEN OPINION OF THE
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International application No.
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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-29
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-29
Industrial applicability (IA)	Yes: Claims	12-20
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and/or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/GB2004/002659

Re Item III**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 1-11 and 21-29 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

Assuming a valid priority of the present application, the P-documents cited in the International search report are not dealt with during the PCT-procedure.

Reference is made to the following documents:

- D1: SCOTT R H ET AL: "Analysis of the structure and electrophysiological actions of halitoxins: 1,3 alkyl-pyridinium salts from *Callyspongia ridleyi*" JOURNAL OF MEMBRANE BIOLOGY 2000 UNITED STATES, vol. 176, no. 2, 2000, pages 119-131, XP002301208 ISSN: 0022-2631
- D2: VAN DER WOUDE I ET AL: "Novel pyridinium surfactants for efficient, nontoxic in vitro gene delivery" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA 1997 UNITED STATES, vol. 94, no. 4, 1997, pages 1160-1165, XP002179111 ISSN: 0027-8424

If not indicated otherwise, the relevant passages are those mentioned in the International search report.

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**WRITTEN OPINION OF THE
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It is clear from the description (see figure 1 b and c and figure 5 a, b and e) that the following features are essential to the definition of the invention (i.e. to obtain a reversible pore formation):

- (1) the molecular weight (see claim 5), and
- (2) the concentration of the sponge toxin (see claim 6)

Furthermore it should be clarified that the present application deals with the formation of pores in cell membranes.

Since independent claims 1, 8, 12 and 21 do not contain these features they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

Art. 33(2) The present application meets the requirements of Article 33(2) PCT, because the subject-matter of **claims 1-29** appears to be new in the sense of Article 33(2) PCT.

None of the cited documents discloses the use of sponge toxins for transient membrane pore formation.

Art. 33(3) The subject-matter of **claims 1-29** is not considered to involve an inventive step in the sense of Article 33(3) PCT.

D1 discloses the use of halitoxin for the formation of irreversible membrane pores, from which the subject-matter of the present application differs in that reversible pores are formed.

The problem to be solved by the present invention may therefore be regarded as how to provide a method for reversible/transient pore formation.

The present application suggests to solve the problem posed by using smaller concentrations of halitoxin.

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Yet, it is known from the teaching of D2 that pyridinium compounds are suitable for efficient transfection by forming membrane pores.

Taking into account the teaching of the cited prior art the following reasoning applies:

With respect to the subject-matter of the remaining **claims 1-29** the applicant's attention is drawn to the fact that there seems to be no basis for inventive step within the present application as filed since no evidence can be found that the features which are novel result in a solution of the posed problem which could not have been foreseen by the skilled person.

Optimizations with respect to amounts only are prima facie obvious.

It is therefore noted, that the solution proposed in **claims 1-29** of the present application is not considered to be inventive in the sense of Article 33(3) PCT.

Art. 33(4) The subject-matter of **claims 12-20** is considered to be industrially applicable in the sense of Art. 33(4) PCT.

For the assessment of the present **claims 1-11 and 21-29** on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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